Clinical presentation, diagnosis, and staging of colorectal cancer

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INTRODUCTION

Colorectal cancer (CRC) is a common and lethal disease. In the United States, approximately 153,000 new cases of large bowel cancer are diagnosed annually [1]. CRC can be diagnosed after the onset of symptoms or through screening asymptomatic individuals.

The clinical presentation, diagnosis, and staging of CRC will be reviewed here. The epidemiology and risk factors, screening and surveillance strategies, pathology and prognostic determinants, and treatment of colon and rectal cancer are discussed elsewhere:

- (See "Colorectal cancer: Epidemiology, risk factors, and protective factors".)
- (See "Surveillance and management of dysplasia in patients with inflammatory bowel disease" and "Screening for colorectal cancer: Strategies in patients at average risk".)
- (See "Screening for colorectal cancer in patients with a family history of colorectal cancer or advanced polyp".)
- (See "Tests for screening for colorectal cancer".)
- (See "Surveillance and management of dysplasia in patients with inflammatory bowel disease" and "Screening for colorectal cancer: Strategies in patients at average risk".)
- (See "Pathology and prognostic determinants of colorectal cancer".)
- (See "Overview of the management of primary colon cancer".)
- (See "Surgical resection of primary colon cancer".)
- (See "Adjuvant therapy for resected stage III (node-positive) colon cancer".)

- (See "Adjuvant therapy for resected stage II colon cancer".)
- (See "Adjuvant therapy for resected colon cancer in older adult patients".)
- (See "Surgical treatment of rectal cancer".)
- (See "Neoadjuvant therapy for rectal adenocarcinoma".)
- (See "Adjuvant therapy for resected rectal adenocarcinoma in patients not receiving neoadjuvant therapy".)

CLINICAL PRESENTATION

Patients with CRC may present in three ways:

- Suspicious symptoms and/or signs
- Asymptomatic individuals discovered by routine screening (see "Screening for colorectal cancer: Strategies in patients at average risk")
- Emergency admission with intestinal obstruction, perforation, or rarely, an acute gastrointestinal bleed

There are no symptoms in the majority of patients with early stage colon cancer and these patients are diagnosed as a result of screening. Although the increasing uptake of CRC screening has led to more cases being diagnosed at an asymptomatic stage, most CRCs (70 to 90 percent in two contemporary series [2,3]) are diagnosed after the onset of symptoms. Symptoms of CRC are typically due to growth of the tumor into the lumen or adjacent structures, and as a result, symptomatic presentation usually reflects relatively advanced CRC. (See "Screening for colorectal cancer: Strategies in patients at average risk" and "Screening for colorectal cancer in patients with a family history of colorectal cancer or advanced polyp".)

Symptoms from the local tumor — Typical symptoms/signs associated with CRC include hematochezia or melena, abdominal pain, otherwise unexplained iron deficiency anemia, and/or a change in bowel habits [4-9]. Less common presenting symptoms include abdominal distention, and/or nausea and vomiting, which may be indicators of obstruction. In a retrospective cohort of over 29,000 patients referred by their general practitioners to an outpatient colorectal surgery clinic over a 22-year period, presenting symptoms in the 1626 who were eventually diagnosed with bowel cancer included [10]:

- Change in bowel habits, which was the most common symptom (74 percent)
- Rectal bleeding in combination with change in bowel habits, which was the most common symptom combination (51 percent of all cancers and 71 percent of those presenting with

rectal bleeding)

- Rectal mass (24.5 percent) or abdominal mass (12.5 percent)
- Iron deficiency anemia (9.6 percent)
- Abdominal pain as a single symptom, which was the least common symptom presentation (3.8 percent)

In more contemporary series, occult anemia seems more common than a change in bowel habits. As an example, in a compilation of the most frequent symptoms and findings that prompted diagnostic colonoscopy in a series of 388 consecutive patients diagnosed with a CRC between 2011 and 2014, the following were noted [2]:

- Blood per rectum (37 percent).
- Abdominal pain (34 percent).
- Anemia (23 percent).
- Six patients (1.9 percent) had incidental colonic hypermetabolic activity detected on a positron emission tomography/computed tomography (PET/CT) image done for another reason.
- Only four individuals (1.3 percent) underwent diagnostic colonoscopy because of change in bowel habits (diarrhea).

Obstructive symptoms are more common with cancers that encircle the bowel, producing the so-called "apple-core" description as seen most classically on barium enema, which is now rarely used (image 1A-B).

Among symptomatic patients, clinical manifestations also differ depending on tumor location:

- A change in bowel habits is a more common presenting symptom for left-sided than right-sided CRCs. Fecal contents are liquid in the proximal colon and the lumen caliber is larger, and CRCs are therefore less likely to be associated with obstructive symptoms, including colicky pain.
- Hematochezia is more often caused by rectosigmoid than right-sided colon cancer.
- Iron deficiency anemia from unrecognized blood loss is more common with right-sided CRCs [11]. Cecal and ascending colon tumors have a fourfold higher mean daily blood loss (approximately 9 mL/day) than tumors at other colonic sites [12]. (See "Causes and

diagnosis of iron deficiency and iron deficiency anemia in adults", section on 'Search for source of blood and iron loss'.)

- Abdominal pain can occur with tumors arising at all sites; it can be caused by a partial obstruction, peritoneal dissemination, or intestinal perforation leading to generalized peritonitis.

- Rectal cancer can cause tenesmus, rectal pain, and diminished caliber of stools.

Risk of cancer based on symptoms — A positive fecal occult blood test has a much higher predictive value that any single or combination of symptoms, warranting a high priority for colonoscopic follow-up.

The risk of CRC posed by particular symptoms has been addressed in the following studies:

- A meta-analysis of 15 studies concluded that the sensitivity of individual symptoms (change in bowel habits, anemia, weight loss, diarrhea, abdominal mass) for the diagnosis of CRC was poor (ranging from 5 to 64 percent) and the specificity was limited, as would be expected for a low-prevalence disease [13]. However, the specificity was >95 percent for dark-red rectal bleeding and for the presence of a palpable abdominal mass on examination, indicating that patients without CRC rarely have these findings and suggesting that the presence of either makes the diagnosis of a CRC likely.

- Another systematic review of 62 studies assessing the relationship between symptoms and CRC used estimates of sensitivity and specificity to calculate a diagnostic odds ratio (DOR = [sensitivity/(1-sensitivity)]/[(1-specificity)/specificity]), which provided a single summary measure of accuracy for each symptom; a high DOR indicates a high correlation between the symptom and the disease, while a DOR of 1 means that the symptom presence is no better than chance in discriminating between diseased and nondiseased patients [14]. The DOR, sensitivity, likelihood ratio of having the disease if the symptom was present, and likelihood of having CRC in the absence of the symptom for a variety of symptoms are outlined in the table (table 1). The authors concluded that only rectal bleeding and weight loss were associated with the presence of CRC, and even these had relatively low DORs.

- A population-based case-control study of clinical features before the diagnosis of CRC conducted in 21 primary care practices in Exeter, Devon, in the United Kingdom included 349 patients over the age of 40 who were diagnosed with CRC over a four-year period and 1744 controls without CRC who were matched by age, sex, and general practice [6]. Primary care records for the two years before diagnosis were reviewed to ascertain

symptoms. Of the 349 cases studied, 210 (60 percent) had tumors at or distal to the splenic flexure and 126 (36 percent) were proximal to it, with the remainder having multiple or unknown sites.

Ten features were associated with CRC before diagnosis; in a univariate analysis, the likelihood ratios for CRC according to symptoms were rectal bleeding 10, weight loss 5.1, abdominal pain 4.5, diarrhea 3.9, constipation 1.8, abnormal rectal examination 18, abdominal tenderness 4.6, hemoglobin <10 g/dL 9.5, and positive fecal occult blood 31. The positive predictive values (PPVs) for abdominal pain, constipation, diarrhea, weight loss, and rectal bleeding were higher for older patients (70 and over), especially rectal bleeding. When symptoms were combined, the PPV was highest (>10) for hemoglobin <10 g/dL combined with abdominal tenderness. The very high PPV for a positive fecal occult blood test validates the policy of prompt investigation of patients with positive fecal occult blood tests, particularly if symptomatic. (See "Tests for screening for colorectal cancer", section on 'Stool-based tests'.)

Role of fecal immunochemical test to triage patients with symptoms — Given the limitations to timely colonoscopy in many health care settings and the nonspecific nature of most colorectal (cancer) symptoms, there is emerging interest in using fecal immunochemical tests for occult blood (FIT) using a low threshold of fecal hemoglobin to maximize sensitivity in order to stratify symptomatic patients who need more urgent diagnostic colonoscopy. This approach is supported by a meta-analysis which concluded that at the lower limit of detection of fecal hemoglobin (≥2 microg/g feces), the summary sensitivity was 97 percent, and the negative predictive value was no lower than 98 percent, regardless of the CRC prevalence [15]. These data suggest that a single quantitative FIT test can adequately exclude CRC in symptomatic patients and allow prioritization of colonoscopy resources, or at least stratification for relative urgency on waiting lists.

However, this approach is not widespread in North America where colonoscopy is readily available. (See "Tests for screening for colorectal cancer", section on 'Stool-based tests'.)

Metastatic disease — Approximately 20 percent of patients in the United States have distant metastatic disease at the time of presentation [1]. CRC can spread by lymphatic and hematogenous dissemination, as well as by contiguous and transperitoneal routes. The most common metastatic sites are the regional lymph nodes, liver, lungs, and peritoneum. Patients may present with signs or symptoms referable to any of these areas. The presence of right upper quadrant pain, abdominal distention, early satiety, supraclavicular adenopathy, or periumbilical nodules usually signals advanced, often metastatic disease.

Because the venous drainage of the intestinal tract is via the portal system, the first site of hematogenous dissemination is usually the liver, followed by the lungs, bone, and many other sites, including the brain. Although brain metastases are exceedingly uncommon, as patients receive more systemic therapy and remain alive for several years after a diagnosis of metastatic cancer there has been an increase in both bone and brain metastases [16]. Tumors arising in the distal rectum may metastasize initially to the lungs rather than liver because the inferior rectal vein drains into the inferior vena cava rather than into the portal venous system.

Unusual presentations — There are a variety of atypical presentations of CRC. These include the following:

- Local invasion or a contained perforation causing malignant fistula formation into adjacent organs, such as bladder (resulting in pneumaturia) or small bowel. This is most common with cecal or sigmoid carcinomas; in the latter case, the condition can mimic diverticulitis.

- Fever of unknown origin, intra-abdominal, retroperitoneal, abdominal wall or intrahepatic abscesses due to a localized perforated colon cancer [17,18]. Streptococcus bovis bacteremia and Clostridium septicum sepsis are associated with underlying colonic malignancies in approximately 10 to 25 percent of patients [19]. Rarely, other extra-abdominal infections caused by colonic anaerobic organisms (eg, Bacteroides fragilis) may be associated with CRC [20]. (See "Infections due to Streptococcus bovis/Streptococcus equinus complex (SBSEC; formerly group D streptococci)", section on 'Association with colonic neoplasia'.)

- CRC ultimately proves to be the site of origin of approximately 6 percent of adenocarcinomas of unknown primary sites [21]. (See "Adenocarcinoma of unknown primary site".)

- CRC may be detected on the basis of discovery of liver metastases that are detected incidentally during studies such as gallbladder or renal ultrasound, or CT scans for evaluation of other symptoms (eg, dyspnea).

Impact of symptoms on prognosis — The presence of symptoms and their particular type provide some prognostic importance:

- Patients who are symptomatic at diagnosis typically have more advanced disease and a worse prognosis [2,22]. In one study of 1071 patients with newly diagnosed colon cancer, 217 of whom were diagnosed through screening, the patients not diagnosed through screening were at higher risk for a more invasive tumor (≥T3: relative risk [RR] 1.96), nodal

involvement (RR 1.92), and metastatic disease on presentation (RR 3.37). In addition, patients not diagnosed through screening had higher risk of death (RR 3.02) and recurrence (RR 2.19) as well as shorter survival and disease-free intervals [22]. (See "Tests for screening for colorectal cancer".)

- The total number of symptoms may be inversely related to survival for colon but not for rectal cancer [23]. Whether the duration of symptoms influences prognosis is unclear; the available data are mixed [24-26].

- Obstruction and/or perforation, although uncommon, carry a poor prognosis, independent of stage [5,27-30]. Among patients with node-negative colon cancer, obstruction or perforation are poor prognostic factors that may influence the decision to pursue adjuvant chemotherapy. (See "Adjuvant therapy for resected stage II colon cancer", section on 'Clinicopathologic features'.)

- Tumors presenting with rectal bleeding (more commonly those involving the distal colon and rectum and at an earlier stage than proximal tumors) have a better prognosis [31,32]. However, bleeding is not an independent predictor of outcome [28,33].

Other determinants of prognosis, including clinicopathologic and molecular features, are discussed elsewhere. (See "Pathology and prognostic determinants of colorectal cancer".)

DIAGNOSIS

The diagnosis of a CRC is made by histologic examination of a biopsy that is usually obtained during lower gastrointestinal tract endoscopy or from a surgical specimen. Histopathologically, the majority of cancers arising in the colon and rectum are adenocarcinomas. The histologic diagnosis of CRC is discussed in detail elsewhere. (See "Pathology and prognostic determinants of colorectal cancer", section on 'Histology'.)

CRC may be suspected from one or more of the symptoms and signs described above or may be asymptomatic and discovered by routine screening of average- and high-risk subjects. Once CRC is suspected, the next test should be colonoscopy or CT colonography. (See "Screening for colorectal cancer: Strategies in patients at average risk" and "Screening for colorectal cancer in patients with a family history of colorectal cancer or advanced polyp" and "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Cancer screening and management" and "Familial adenomatous polyposis: Screening and management of patients and families" and "Juvenile polyposis syndrome".)

Colonoscopy — Colonoscopy is the most accurate and versatile diagnostic test for CRC, since it can localize and biopsy lesions throughout the large bowel, detect synchronous neoplasms, and remove polyps. Synchronous CRCs, defined as two or more distinct primary tumors diagnosed within six months of an initial CRC, separated by normal bowel, and not due to direct extension or metastasis, occur in 3 to 5 percent of patients [34-36]. The incidence is somewhat lower (approximately 2.5 percent) when patients with Lynch syndrome are excluded; the presence of synchronous cancers should raise the clinical suspicion for Lynch Syndrome or MUTYH-associated polyposis [37,38]. (See "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Clinical manifestations and diagnosis", section on 'Colonic manifestations'.)

The preparation for, diagnostic use of, and complications associated with colonoscopy are discussed elsewhere. (See "Overview of colonoscopy in adults".)

When viewed through the endoscope, the vast majority of colon and rectal cancers are endoluminal masses that arise from the mucosa and protrude into the lumen (figure 1). The masses may be exophytic or polypoid. Bleeding (oozing or frank bleeding) may be seen with lesions that are friable, necrotic, or ulcerated (picture 1A-B).

A minority of neoplastic lesions in the gastrointestinal tract (both in asymptomatic and symptomatic individuals) are nonpolypoid and relatively flat or depressed. In one study, nonpolypoid colorectal neoplasms had a greater association with carcinoma than did polypoid neoplasms [39]. Cancers that arise from nonpolypoid (flat) adenomas may be more difficult to visualize colonoscopically than polypoid lesions, but colonoscopy has superior sensitivity to CT colonography in this situation.

For endoscopically visible lesions, methods for tissue sampling include biopsies and polypectomy. For lesions that are completely removed endoscopically (with polypectomy, endoscopic mucosal resection, or endoscopic submucosal dissection), tattooing is important for subsequent localization if an invasive neoplasm is found, and additional local therapy is needed. Tattoos are typically placed adjacent to or just centimeters distal to the lesion, being careful not to include the lesion in the tattoo, with the location being documented in the colonoscopy report. Large, laterally spreading colonic polyps can now be safely removed endoscopically, provided they meet endoscopic criteria that predict their noninvasive nature (table 2). (See "Tattooing and other methods for localizing gastrointestinal lesions" and "Endoscopic removal of large colon polyps", section on 'Patient selection'.)

Among asymptomatic patients, colonoscopy miss rates for CRCs in the hands of experienced operators range from 2 to 6 percent, and missed cancers are most frequently on the right side of the colon [40-43].

The available data concerning miss rates for CRC among symptomatic patients undergoing colonoscopy are as follows:

- In a systematic review and meta-analysis of 25 diagnostic studies providing data on 9223 patients with a cumulative CRC prevalence of 3.6 percent (414 cancers), the sensitivity of optical colonoscopy for detection of CRC was 94.7 percent (178 of 188, 95% CI 90-97.2) [44]. Thus, the miss rate was 5.3 percent.

- Large retrospective studies from Canada [45-47] and the United States [48-50] have used administrative databases to identify patients diagnosed with CRC who had had a colonoscopy performed for any indication 6 to 60 months prior to CRC diagnosis. These interval, missed, or post-colonoscopy CRCs accounted for 6 to 9 percent of all CRCs in their series. Other studies of post-colonoscopy CRC (sometimes called interval cancers) have shown a close inverse relationship between the incidence of these cancers in a colonoscopist's practice and that colonoscopist's adenoma detection rate. (See "Overview of colonoscopy in adults", section on 'Quality indicators'.)

If a malignant obstruction precludes a full colonoscopy preoperatively, the entire residual colon should be examined soon after resection.

In the absence of an obstruction, where colonoscopy is incomplete, additional options include CT colonography or Pill Cam colon 2, a wireless colon video endoscopy capsule approved for CRC screening, although its use in patients with symptoms suggestive of CRC (eg, anemia, rectal bleeding, weight loss) is controversial. (See 'Computed tomography colonography' below and 'PILLCAM 2' below and "Tests for screening for colorectal cancer", section on 'Colon capsule endoscopy' and "Wireless video capsule endoscopy", section on 'Colon capsule endoscopy' and "Overview of computed tomographic colonography".)

Flexible sigmoidoscopy — Over the last 50 years, a gradual shift toward right-sided or proximal colon cancers has been observed both in the United States and internationally, with the greatest increase in incidence in cecal primaries (picture 2). Because of this, and because of the high frequency of synchronous CRCs, flexible sigmoidoscopy is generally not considered to be an adequate diagnostic study for a patient suspected of having a CRC, unless a palpable mass is felt in the rectum. In such cases, a full colonoscopy will still be needed to evaluate the remainder of the colon for synchronous polyps and cancers (see "Colorectal cancer: Epidemiology, risk factors, and protective factors", section on 'Incidence'). Nevertheless, screening for CRC using a flexible sigmoidoscope is one of the few modalities that have been proven through randomized controlled trials to reduce CRC mortality and incidence [51].

Computed tomography colonography — CT colonography (also called virtual colonoscopy or CT colography) provides a computer-simulated endoluminal perspective of the air-filled distended colon. The technique uses conventional spiral or helical CT scan or, in the case of magnetic resonance colonography, magnetic resonance images acquired as an uninterrupted volume of data and employs sophisticated postprocessing software to generate images that allow the operator to fly through and navigate a cleansed colon in any chosen direction. CT colonography requires a mechanical bowel preparation that is similar to that needed for barium enema, since stool can simulate polyps. (See "Overview of computed tomographic colonography".)

CT colonography has been evaluated in patients with incomplete colonoscopy and as an initial diagnostic test in patients with symptoms suggestive of CRC.

Incomplete colonoscopy — Non-completion rates for diagnostic colonoscopy in symptomatic patients are approximately 11 to 12 percent [51,52]. Reasons for incompleteness include the inability of the colonoscope to reach the tumor or to visualize the mucosa proximal to the tumor for technical reasons (eg, partially or completely obstructing cancer, tortuous colon, poor preparation) and patient intolerance of the examination. In this setting, CT colonography is useful for the detection of CRC and can provide a radiographic diagnosis, although it can overcall stool as masses in poorly distended or poorly prepared colons; it also lacks the capability for biopsy or removal of polyps [44,53-56].

CT colonography should be restricted to patients who are able to pass flatus and capable of tolerating the oral preparation. For clinically obstructed patients, a gastrointestinal protocol abdominal CT scan is a good alternative to CT colonography.

Initial diagnostic test — Systematic reviews of screening studies conducted in asymptomatic patients suggest that both CT colonography and colonoscopy have similar diagnostic yield for detecting CRC and large polyps. Comparison of the benefits and costs of the two procedures depends on other factors, one of the most important of which is the need for additional investigation after CT colonography and the exposure to radiation, which is particularly important where recurrent scanning over time may be contemplated such as in screening. (See "Radiation-related risks of imaging".)

Abnormal results with CT colonography should be followed up by colonoscopy for excision and tissue diagnosis, or for smaller lesions, additional surveillance with CT colonography. There is controversy as to the threshold size of a polyp that would indicate the need for (interventional) colonoscopy and polypectomy. CT colonography also has the ability to detect extracolonic lesions, which might explain symptoms and provide information as to the tumor stage, but also

could generate anxiety and cost for unnecessary investigation and may have a low yield of clinically important pathology [57]. (See "Tests for screening for colorectal cancer", section on 'Computed tomography colonography'.)

The performance of diagnostic CT colonography as compared with colonoscopy in patients with symptoms suggestive of CRC has been addressed in the following studies:

- A systematic review and meta-analysis included 49 studies (11,551 patients) in which patients underwent CT colonography for the diagnosis of colorectal polyps and cancer with subsequent colonoscopy for verification of the findings; 43 studies (6668 patients) examined a symptomatic or disease-enriched population [44]. There were 394 cancers in the symptomatic population (prevalence 6 percent) and a total of 414 cancers in the entire cohort. CT colonography detected 96.1 percent of the histologically proven cancers (95% CI 93.9-97.7 percent). In a subset of 25 studies (9223 patients) in which the sensitivity of colonoscopy could be assessed independently (ie, when the colonoscopy was performed without knowledge of the prior CT colonography result, an analysis which included predominantly data from asymptomatic individuals), the sensitivity of colonoscopy was 94.7 percent (178 of 188 cancers, 95% CI 90.4-97.2 percent).

- The diagnostic performance of CT colonography was directly compared with colonoscopy in the SIGGAR (Special Interest Group in Gastrointestinal and Abdominal Radiology) trial in which 1610 patients with symptoms suggestive of CRC were randomly assigned to colonoscopy (n = 1072) or CT colonography (n = 538) [51]. The primary endpoint was the rate of additional colonic investigation after the primary procedure for detection of CRC or large (>10 mm) polyps. Detection rates for CRC and large polyps were 11 percent for both procedures. CT colonography missed 1 of 29 CRCs and colonoscopy missed none of 55. However, patients undergoing CT colonography were more than three times more likely to get additional colonic investigations (30 versus 8 percent). Only one-third of the patients who underwent additional investigations were found to have CRC or a large polyp.

  At least one previously unknown extracolonic finding was reported in 60 percent of the 475 patients who had CT colonography and no diagnosis of CRC. Most were judged to be clinically unimportant. Among the 48 patients who were investigated further for extracolonic findings, only approximately one-third received a diagnosis that explained at least one of their presenting symptoms and only nine patients were found to have an extracolonic malignancy.

  Overall, CT colonography had superior patient acceptability compared with colonoscopy in the short term (immediately after the test) but the benefits of colonoscopy (being more

satisfied with how results were received and less likely to require follow-up colonic investigations) became apparent after longer-term follow-up (three months) [58].

The available data suggest that CT colonography provides a similarly sensitive, less invasive alternative to colonoscopy in patients presenting with symptoms suggestive of CRC. CT colonography may be particularly valuable in patients with an obstructing CRC with the ability to tolerate a bowel preparation. In one study, performing a CT colonography led to a change in the surgical plan because of the presence of synchronous tumors in 1.4 percent of cases [59]. However, given that colonoscopy permits removal/biopsy of the lesion and any synchronous cancers or polyps that are seen during the same procedure, in our view, colonoscopy remains the gold standard for investigation of symptoms suggestive of CRC. CT colonography is preferred over barium enema where access to colonoscopy is limited.

PILLCAM 2 — A colon capsule for CRC screening has been approved by the European Medicines Agency (EMA) in Europe and by the US Food and Drug Administration (FDA). In the United States, it is approved for use in patients who have had an incomplete colonoscopy. While its role in screening for CRC is still uncertain, it could be considered in a patient with an incomplete colonoscopy who lacks obstruction.

Laboratory tests — Although CRC is often associated with iron deficiency anemia, its absence does not reliably exclude the disease. There is no diagnostic role for other routine laboratory test, including liver function tests, which lack sensitivity for detection of liver metastases.

Tumor markers — A variety of serum markers have been associated with CRC, particularly carcinoembryonic antigen (CEA). However, all these markers, including CEA, have a low diagnostic ability to detect primary CRC due to significant overlap with benign disease and low sensitivity for early stage disease [60-62]. A meta-analysis concluded that the pooled sensitivity of CEA for diagnosis of CRC was only 46 percent (95% CI 0.45-0.47) [63]. No other conventional tumor marker had a higher diagnostic sensitivity, including carbohydrate antigen 19-9 (CA 19-9, pooled sensitivity 0.30, 95% CI 0.28-0.32).

Furthermore, specificity of CEA is also limited. In the previously mentioned meta-analysis, the specificity of CEA for diagnosis of CRC was 89 percent (95% CI 0.88-0.92). Non-cancer-related causes of an elevated CEA include gastritis, peptic ulcer disease, diverticulitis, liver disease, chronic obstructive pulmonary disease, diabetes, and any acute or chronic inflammatory state. In addition, CEA levels are significantly higher in cigarette smokers than in non-smokers [64,65].

Because of these issues, neither serum CEA nor any other marker, including CA 19-9, should be used as a screening or diagnostic test for CRC.

However, CEA levels do have value in the prognosis and follow-up of patients with diagnosed CRC:

- Serum levels of CEA have prognostic utility in patients with newly diagnosed CRC. Patients with preoperative serum CEA >5 ng/mL have a worse prognosis, stage for stage, than those with lower levels, although at least some data suggest that elevated preoperative CEA that normalizes after resection is not an indicator of poor prognosis [66]. (See "Pathology and prognostic determinants of colorectal cancer", section on 'Preoperative serum CEA'.)

- Elevated preoperative CEA levels that do not normalize following surgical resection imply the presence of persistent disease and the need for further evaluation. (See "Post-treatment surveillance after colorectal cancer treatment", section on 'Carcinoembryonic antigen'.)

Furthermore, serial assay of postoperative CEA levels should be performed for five years for patients with stage II and III disease if they may be a potential candidate for surgery or chemotherapy if metastatic disease is discovered. A rising CEA level after surgical resection implies recurrent disease and should prompt follow-up radiologic imaging. (See "Post-treatment surveillance after colorectal cancer treatment".)

Other blood tests — Blood-based tests for early detection of CRC, or to monitor for postoperative recurrence, are under active development at present. Amongst the contenders are methylated circulating DNA markers [67-71] and blood-based microRNAs, as well as other emerging cell-free DNA approaches such as multicancer early detection tests [72,73]. (See "Tests for screening for colorectal cancer", section on 'Blood-based markers'.)

DIFFERENTIAL DIAGNOSIS

The signs and symptoms associated with CRC are nonspecific, and the differential diagnosis, particularly among patients presenting with abdominal pain and rectal bleeding, is broad. (See "Causes of abdominal pain in adults" and "Etiology of lower gastrointestinal bleeding in adults" and "Evaluation of occult gastrointestinal bleeding" and "Approach to acute lower gastrointestinal bleeding in adults".)

Many conditions cause signs or symptoms that are similar to colorectal adenocarcinomas including other malignancies as well as benign lesions such as hemorrhoids, diverticulitis, infection, or inflammatory bowel disease.

The differential diagnosis of a colonic mass as seen on radiographic or endoscopic studies includes a number of benign and malignant disorders, the differentiation of which generally requires biopsy and histologic evaluation (table 3). In particular, rare malignancies other than adenocarcinomas that are primary to the large bowel include Kaposi sarcoma (KS), gastrointestinal stromal tumors, lymphomas, carcinoid (well-differentiated neuroendocrine) tumors, and metastases from other primary cancers. (See "Pathology and prognostic determinants of colorectal cancer", section on 'Histology'.)

- Disseminated KS can involve the colon, particularly in patients with AIDS, manifested as characteristic violaceous macules or nodules [74]. (See "AIDS-related Kaposi sarcoma: Clinical manifestations and diagnosis", section on 'Gastrointestinal tract'.)

- Primary non-Hodgkin lymphoma of the large bowel most commonly arises in the cecum, right colon, or rectum and usually presents at an advanced stage in adults. Colonic lymphoma typically appears as a large solitary mass, although multiple polypoid lesions or diffuse involvement can occur [75]. (See "Clinical presentation and diagnosis of primary gastrointestinal lymphomas".)

- Colonic carcinoid tumors are found most commonly in the appendix, rectum, and cecum, and they tend to develop at a younger age than adenocarcinomas of the colon. Appendiceal and rectal carcinoids, most of which are less than 2 cm, appear as submucosal nodules and tend to be indolent. In contrast, primary colonic carcinoid tumors can present as large apple-core lesions, which can be clinically aggressive and may metastasize. (See "Clinical characteristics of well-differentiated neuroendocrine (carcinoid) tumors arising in the gastrointestinal and genitourinary tracts".)

- Gastrointestinal stromal tumors develop in the wall of the gastrointestinal tract from interstitial cells of Cajal. Other mural tumors that derive from smooth muscle include a spectrum of histologic characteristics that range from slow growing with low mitotic activity (classified as leiomyomas) to faster growing tumors with very high mitotic activity (designated as leiomyosarcomas). (See "Clinical presentation, diagnosis, and prognosis of gastrointestinal stromal tumors" and "Local treatment for gastrointestinal stromal tumors, leiomyomas, and leiomyosarcomas of the gastrointestinal tract".)

- Metastases from other primary cancers, most often ovarian cancer, can mimic a primary large bowel malignancy. (See "Epithelial carcinoma of the ovary, fallopian tube, and peritoneum: Clinical features and diagnosis", section on 'Differential diagnosis'.)

STAGING

Once the diagnosis of CRC is established, the local and distant extent of disease is determined to provide a framework for discussing therapy and prognosis. A review of the biopsy specimen is important prior to making a decision about the need for clinical staging studies and surgical resection, especially for a cancerous polyp. Polyps with an area of invasive malignancy that have been completely removed and lack associated adverse histologic features (positive margin, poor differentiation, lymphovascular invasion) have a low risk of lymphatic and distant metastases; in such patients, polypectomy alone may be adequate. This is more easily determined if the polyp is pedunculated. (See "Overview of colon polyps".)

TNM staging system — The Tumor, Node, Metastasis (TNM) staging system of the combined American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) is the preferred staging system for CRC. Use of the older Astler-Coller modification of the Duke's classification is discouraged.

The most recent (eighth edition, 2017) revision of the TNM staging classification contains few changes compared with the earlier 2010 seventh edition (table 4) [76]. The M1c stage has been introduced to reflect peritoneal carcinomatosis as a poor prognostic factor, and nodal micrometastases (tumor clusters >0.2 mm in diameter) are now scored as positive given the results of a meta-analysis demonstrating a poor prognosis in these patients [77]. (See "Pathology and prognostic determinants of colorectal cancer", section on 'Nodal micrometastases'.)

In addition, the definition of tumor deposits as they apply to regional nodal status is clarified. This version also acknowledges the following factors, which are important to consider when making decisions about treatment but are not yet incorporated into the formal staging criteria:

- Preoperative serum carcinoembryonic antigen (CEA) levels. (See 'Tumor markers' above.)
- Tumor regression score, which reflects the pathologic response to preoperative radiotherapy, chemoradiotherapy, or chemotherapy (table 5) and the status of the circumferential resection margin for rectal cancers. (See "Pathology and prognostic determinants of colorectal cancer", section on 'Circumferential (radial) margin' and "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Prognosis and extent of tumor regression'.)
- Lymphovascular and perineural invasion. (See "Pathology and prognostic determinants of colorectal cancer", section on 'Lymphovascular invasion' and "Pathology and prognostic

determinants of colorectal cancer", section on 'Perineural invasion'.)

- Microsatellite instability, which reflects deficiency of mismatch repair enzymes and is both a good prognostic factor and predictive of a lack of response to fluoropyrimidine therapy. It also identifies patients who might be responsive to checkpoint inhibitors in the setting of advanced metastatic disease. (See "Pathology and prognostic determinants of colorectal cancer", section on 'Mismatch repair deficiency'.)

- Mutation status of *KRAS*, *NRAS*, and *BRAF*, because mutations in these genes are associated with lack of response to agents targeting the epidermal growth factor receptor (EGFR). (See "Pathology and prognostic determinants of colorectal cancer", section on 'RAS and BRAF'.)

However, this TNM staging classification is not used in all countries. As examples, in some areas of the Netherlands, the fifth edition of the TNM staging classification is still used purposely for rectal cancer, as later modifications were not considered to represent an improvement, whereas in Japan, none of the revised criteria on satellite deposits that lack evidence of a residual lymph node were adopted in the most current seventh (2006) edition of the National Cancer Staging Manual edited by the Japanese Society for Cancer of the Colon and Rectum because of the lack of sufficient justification for this change [78].

Radiographic, endoscopic (including biopsy), and intraoperative findings can be used to assign a clinical stage, while assessment of the pathologic stage (termed pT, pN, pM) requires histologic examination of the resection specimen. Preoperative radiation and chemotherapy (as are often undertaken for locally advanced rectal cancer) can significantly alter clinical staging; as a result, posttherapy pathologic staging is designated with a yp prefix (ie, ypT, ypN). (See "Pathology and prognostic determinants of colorectal cancer", section on 'Posttherapy staging for rectal cancer'.)

Clinical staging evaluation — Preoperative clinical staging is best accomplished by physical examination (with particular attention to ascites, hepatomegaly, and lymphadenopathy, and potential fixation of rectal cancers); CT scan of the chest, abdomen, and pelvis; and magnetic resonance imaging (MRI) of the pelvis for rectal cancer. (See "Pretreatment local staging evaluation for rectal cancer".)

Although frequently obtained preoperatively, liver enzymes may be normal in the setting of small hepatic metastases and are not a reliable marker for exclusion of liver involvement (picture 3). The single most common liver test abnormality associated with liver metastases is an elevation in the serum alkaline phosphatase level [79].

Computed tomography scan — In the United States and elsewhere, the standard practice at most institutions is that all patients with stage II, III, or IV CRC undergo chest, abdomen, and pelvic CT, either prior to or following resection, an approach endorsed by the National Comprehensive Cancer Network [80]. In general, it is preferable to obtain these scans prior to, rather than after surgery, as the scan results will occasionally change surgical planning.

Abdomen and pelvis — In patients with newly diagnosed CRC, preoperative abdominal and pelvic CT scans can demonstrate regional tumor extension, regional lymphatic and distant metastases, and tumor-related complications (eg, obstruction, perforation, fistula formation) [81,82]. The sensitivity of CT for detecting distant metastasis is higher (75 to 87 percent) than for detecting nodal involvement (45 to 73 percent) or the depth of transmural invasion (approximately 50 percent) [81,83-88]. The sensitivity of CT for detection of malignant lymph nodes is higher for rectal than for colon cancers; perirectal adenopathy is presumed to be malignant since benign adenopathy is typically not seen in this area in the absence of demonstrable inflammatory process (eg, proctitis, fistula, perirectal abscess) [89]. However, pelvic MRI provides a better assessment of clinical tumor and nodal stage as well as proximity of the tumor to the circumferential resection margin, and is considered the gold standard for rectal cancer staging. This subject is discussed elsewhere. (See "Pretreatment local staging evaluation for rectal cancer".)

CT scan is not a reliable diagnostic test for low-volume tumor on peritoneal surfaces [90]. The sensitivity of CT for detecting peritoneal implants depends on the location and size of the implants. In one study, the sensitivity of CT for nodules <0.5 cm was 11 percent and it was only 37 percent for implants 0.5 to 5 cm [91].

Although commonly obtained, the necessity of preoperative abdominal/pelvic CT for all patients with CRC is debated. In a retrospective review of 180 resected patients, only 3 of 67 patients had incidental findings on CT that altered the surgical approach [86]. Assessment of hepatic metastases by intraoperative ultrasound and manual palpation of the liver may provide a better yield than preoperative CT, particularly for patients who are found to have transmural involvement (T3/4) at the time of exploration [92-94]. However, the increasing use of laparoscopic colonic resections precludes manual palpation, and even with open procedures surgeons may not have adequate access to the liver depending on the location of the incision and the extent of adhesions from prior surgery.

The finding of liver metastases on preoperative studies may not necessarily alter the surgical approach to the primary tumor, particularly in patients who are symptomatic from their primary tumor (eg, bleeding, impending obstruction). In patients with four or fewer hepatic lesions, resection may be curative, with five-year relapse-free survival rates of 24 to 38 percent.

Although most surgeons advocate resection of the primary tumor and synchronous hepatic metastases at two different operations, some approach both sites at the same time. (See "Potentially resectable colorectal cancer liver metastases: Integration of surgery and chemotherapy".)

Chest — The clinical benefit of routine clinical staging with chest CT is also controversial. At least in theory, imaging of the chest might be of more value for rectal cancer since venous drainage of the lower rectum is through the hemorrhoidal veins to the vena cava, bypassing the liver, and lung metastases might be more common [95].

The major issue is the frequent finding of indeterminate lesions (10 to 30 percent), which add to the clinical complexity (ie, should further preoperative diagnostic workup be undertaken) but are seldom malignant (7 to 20 percent). A systematic review of 12 studies including 5873 patients undergoing staging for a newly diagnosed CRC [96] found that 732 (9 percent) had indeterminate pulmonary nodules on preoperative chest CT. Of these, 80 (11 percent) turned out to be colorectal metastases at follow-up. Generally, the presence of regional nodal metastases at the time of resection, multiple numbers of indeterminate pulmonary nodules, size ≥5 mm, rectal as compared with colon cancer, parenchymal versus subpleural location of the nodule, and distant metastases elsewhere were significantly associated with malignancy, while calcification was associated with a benign etiology. Overall, the risk of malignancy for most patients with indeterminate pulmonary nodules (approximately 1 percent) seems sufficiently low that further preoperative diagnostic workup is unnecessary.

Liver magnetic resonance imaging — Contrast-enhanced MRI of the liver can identify more hepatic lesions than are visualized by CT and is particularly valuable in patients with background fatty liver changes [97]. A meta-analysis concluded that MRI is the preferred first-line imaging study for evaluating CRC liver metastases in patients who have not previously undergone therapy [98]. However, newer-generation CT scanners and the use of triple-phase imaging during contrast administration has improved sensitivity of CT for detection of liver metastases. In current practice, liver MRI is generally reserved for patients who have suspicious but not definitive findings on CT scan, particularly if better definition of hepatic disease burden is needed in order to make decisions about potential hepatic resection. (See "Potentially resectable colorectal cancer liver metastases: Integration of surgery and chemotherapy".)

Positron emission tomography scans — Positron emission tomography (PET) scans with or without integrated CT (PET/CT) do not appear to add significant information to CT scans for routine preoperative staging of CRC [99-101]. The established role of PET scanning in patients with CRC as an adjunct to other imaging modalities is described in the following settings:

- Localizing site(s) of disease recurrence in patients who have a rising serum CEA level and nondiagnostic conventional imaging evaluation following primary treatment. In this setting, PET scanning can potentially localize occult disease, permitting the selection of patients who may benefit from exploratory laparotomy [102-105]. (See "Post-treatment surveillance after colorectal cancer treatment".)

  In an illustrative series, 105 such patients underwent PET scanning and subsequent abdominopelvic CT scans [102]. Compared with CT and other conventional diagnostic studies, PET scanning had a higher sensitivity (87 versus 66 percent) and specificity (68 versus 59 percent) for the detection of clinically relevant tumor. In a second report, PET scan findings led to a potentially curative resection in 14 of 50 patients (28 percent) with elevated serum CEA levels and a completely normal or equivocal conventional diagnostic workup [103].

- Evaluation of patients who are thought to be present or future candidates for resection of isolated CRC liver metastases. The routine use of PET prior to attempted resection reduces the number of nontherapeutic laparotomies, but the impact on long-term outcomes is uncertain. As an example, in one randomized trial, routine preoperative evaluation of potentially resectable CRC liver metastases with PET-CT resulted in a change in surgical management in 8 percent of patients, but there was no effect on recurrence rates or long-term survival [106].

  An important point is that recent chemotherapy may alter the sensitivity of PET for the detection of colorectal liver metastases, an effect thought related to decreased cellular metabolic activity of the tumor. However, generally, the benefit of a PET scan is to detect extrahepatic metastases in patients considered liver resection candidates, and in this situation, it is appropriate to obtain a PET prior to initiation of chemotherapy. This subject is addressed in detail elsewhere. (See "Hepatic resection for colorectal cancer liver metastasis", section on 'Positron emission tomography' and "Potentially resectable colorectal cancer liver metastases: Integration of surgery and chemotherapy", section on 'Pretreatment considerations'.)

Locoregional staging for rectal cancer — An accurate determination of tumor location within the rectum and disease extent is necessary prior to treatment in order to select the surgical approach and to identify those patients who are candidates for initial chemoradiotherapy prior to surgery. (See "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Indications for neoadjuvant treatment'.)

Digital rectal examination (DRE), rigid sigmoidoscopy, transrectal ultrasound, transrectal endoscopic ultrasound, and pelvic MRI can all assist in determining the need for radical resection versus local excision, and whether the patient is a candidate for preoperative therapy. This subject is discussed elsewhere. (See "Pretreatment local staging evaluation for rectal cancer".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Colorectal cancer".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Colon and rectal cancer (The Basics)")
- Beyond the Basics topics (see "Patient education: Colon and rectal cancer (Beyond the Basics)" and "Patient education: Colorectal cancer treatment; metastatic cancer (Beyond the Basics)")

SUMMARY

- **Clinical presentation**
  - Patients with colorectal cancer (CRC) may present in three ways (see 'Clinical presentation' above):

- The presence of suspicious symptoms and/or signs
- Asymptomatic individuals discovered by routine screening or as a result of findings from a radiographic study done for another purpose
- Emergency admission with intestinal obstruction, peritonitis, or rarely, an acute gastrointestinal bleed

- Most CRCs are diagnosed after the onset of symptoms (most commonly rectal bleeding, abdominal pain, otherwise unexplained iron deficiency anemia, and/or a change in bowel habits). A change in bowel habits is a more common presenting symptom for left-sided as compared with right-sided cancers. Hematochezia is more likely with rectal than colon cancers, and occult colonic bleeding is more common with cecal and ascending colon cancers. (See 'Symptoms from the local tumor' above.)

  A positive fecal occult blood test has a much higher predictive value that any single or combination of symptoms, warranting a high priority for colonoscopic follow-up. (See 'Risk of cancer based on symptoms' above.)

  One in five patients with CRC presents with metastatic disease, with the most common sites being regional lymph nodes, liver, lungs, and peritoneum. (See 'Metastatic disease' above.)

  Unusual presentations of CRC include malignant fistula formation, fever of unknown origin, sepsis from *Streptococcus bovis* and *Clostridium septicum*, and adenocarcinoma of unknown primary. (See 'Unusual presentations' above.)

- **Diagnosis**

  - The vast majority of CRCs are endoluminal adenocarcinomas that arise from the mucosa. The diagnosis is made by histologic examination of a biopsy that is usually obtained during lower gastrointestinal tract endoscopy or from a surgical specimen. (See 'Diagnosis' above.)
  - Colonoscopy is the most versatile diagnostic test in symptomatic individuals. (See 'Colonoscopy' above.)
  - CT colonography provides a similarly sensitive, less invasive alternative to colonoscopy in patients presenting with symptoms suggestive of CRC. However, colonoscopy is preferred as it permits removal/biopsy of the lesion and any synchronous cancers or polyps that are seen during the same procedure. (See 'Initial diagnostic test' above.)

For patients in whom, for technical reasons, the tumor cannot be reached by colonoscopy (eg, partially obstructing cancer, tortuous colon, poor preparation) or because of patient intolerance, CT colonography can provide a radiographic diagnosis, but without the capability for biopsy or removal of polyps. (See 'Computed tomography colonography' above.)

CT colonography is preferred over barium enema where access to colonoscopy is limited.

- There is no diagnostic role for routine laboratory testing in screening or staging CRC. However, serum carcinoembryonic antigen (CEA) levels should be obtained preoperatively and postoperatively in patients with demonstrated CRC to aid surgical treatment planning and assessment of prognosis. (See 'Tumor markers' above.)

- **Staging**

  - Once the diagnosis is established, the local and distant extent of disease spread is determined to provide a framework for discussing therapy and prognosis. Preoperative clinical staging is best accomplished by physical examination, CT scan of the abdomen and pelvis, and chest imaging. (See 'Clinical staging evaluation' above.)

    Positron emission tomography (PET) scans do not appear to add significant information to CT scans for routine preoperative staging of a newly diagnosed CRC except for the evaluation of patients who are thought to be candidates for resection of isolated CRC liver metastases. (See 'Positron emission tomography scans' above.)

  - Additional procedures (digital rectal examination [DRE], rigid sigmoidoscopy, transrectal endoscopic ultrasound, and/or MRI) are indicated for locoregional staging of patients with rectal cancer to select the surgical approach and to identify those patients who are candidates for initial radiotherapy or chemoradiotherapy rather than surgery. (See 'Locoregional staging for rectal cancer' above.)

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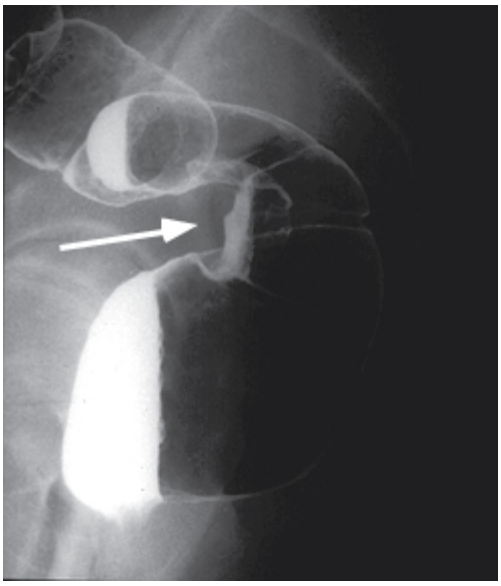
Topic 2496 Version 86.0

GRAPHICS

Rectal cancer as seen on barium enema

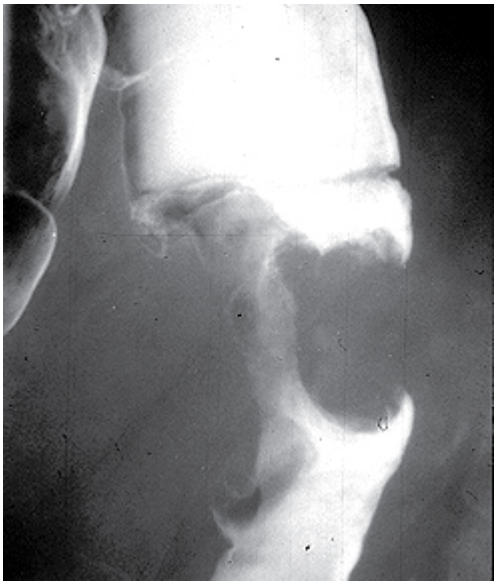


Double-contrast barium enema shows an eccentric mass arising from the anterior wall of the rectum (arrow).

Courtesy of Jonathan Kruskal, MD, PhD.

Graphic 82202 Version 3.0

Cancer of the colon as seen on barium enema



Double contrast barium enema shows an apple-core lesion surrounding the lumen of the descending colon.

Courtesy of Jonathan Kruskal, MD.

Graphic 75818 Version 3.0

Symptoms associated with colorectal cancer

Symptom	DOR* (95% CI*)	AUC¶	Sensitivity (95% CI)	1-specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)
Rectal bleeding[Δ]	2.6 (1.9-3.6) p<0.001	0.66	0.46 (0.38-0.55)	0.25 (0.19-0.31)	1.9 (1.5-2.3)	0.7 (0.6-0.8)
Blood mixed with stool	3.1 (2.0-4.8) p<0.001	0.68	0.49 (0.30-0.69)	0.24 (0.13-0.40)	2.1 (1.5-2.8)	0.7 (0.5-0.9)
Blood: dark red	3.9 (1.7-9.2) p = 0.004	0.71	0.29 (0.09-0.65)	0.10 (0.03-0.28)	3.1 (1.6-6.0)	0.8 (0.6-1.1)
Change in bowel habit	1.5 (0.8-2.8) p = 0.16	0.57	0.32 (0.21-0.46)	0.24 (0.15-0.35)	1.4 (0.9-2.1)	0.9 (0.7-1.1)
Constipation	1.1 (0.8-1.5) p = 0.48	0.52	0.12 (0.08-0.18)	0.11 (0.07-0.16)	1.1 (0.8-1.5)	1.0 (1.0-1.0)
Diarrhea	0.9 (0.4-1.7) p = 0.65	0.47	0.15 (0.07-0.28)	0.17 (0.09-0.29)	0.9 (0.5-1.6)	1.0 (0.9-1.1)
Abdominal pain	0.7 (0.5-1.1) p = 0.12	0.45	0.19 (0.13-0.28)	0.24 (0.17-0.33)	0.8 (0.6-1.1)	1.1 (1.0-1.2)
Weight loss	2.9 (1.6-5.0) p = 0.001	0.67	0.20 (0.12-0.31)	0.08 (0.05-0.13)	2.5 (1.5-4.0)	0.9 (0.8-1.0)

LR+: the likelihood ratio of having colorectal cancer in the presence of the symptom; LR–: the likelihood ratio of having colorectal cancer in the absence of the symptom.

* DOR: diagnostic odds ratio. No association between symptom and cancer if DOR = 1.

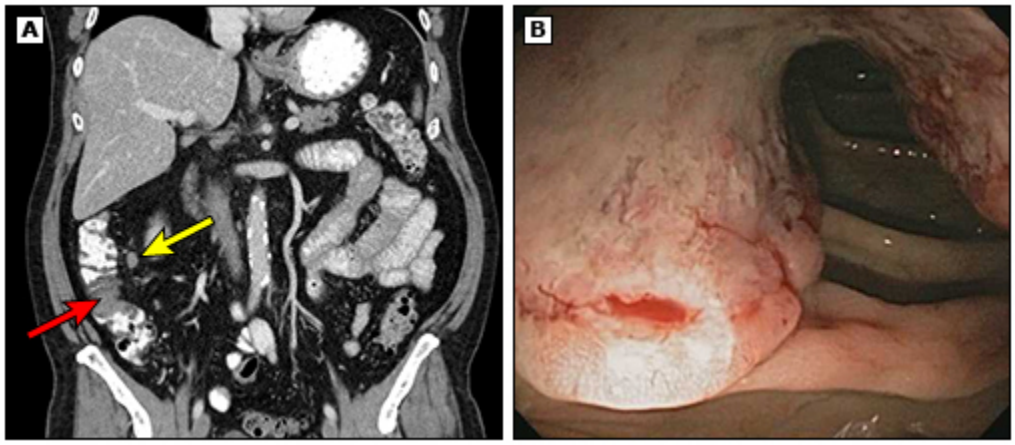
¶ AUC: Area Under the receiver operating characteristic Curve. No association between symptom and cancer if AUC = 0.5.

Δ Bleeding of any type.

Reproduced from: Adelstein B, Macaskill P, Chan SF, et al. Most bowel cancer symptoms do not indicate colorectal cancer and polyps: a systematic review. BMC Gastroenterology 2011; 11:65. Copyright © 2011 Adelstein et al.

Graphic 88734 Version 4.0

Colon cancer seen on CT scan and colonoscopy

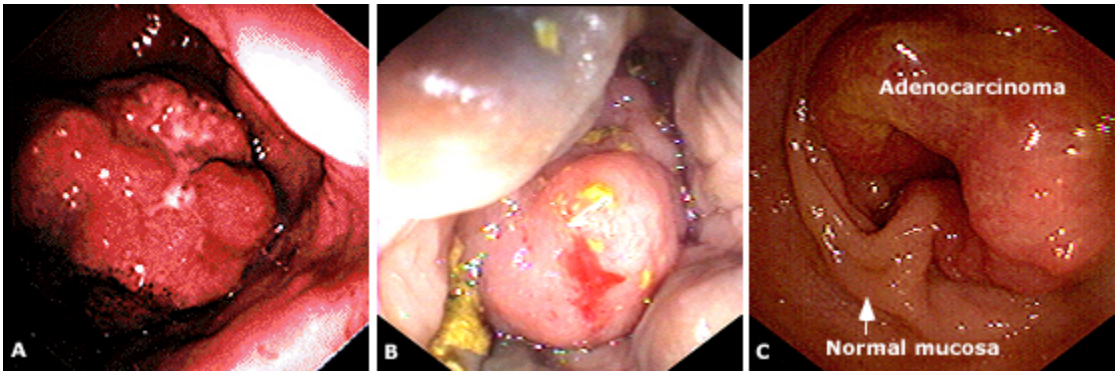


(A) Computed tomographic (CT) scan showing a filling defect in the ascending colon (red arrow) along with an involved lymph node (yellow arrow).

(B) Colon cancer identified in the ascending colon on subsequent colonoscopy.

Graphic 83618 Version 1.0

Adenocarcinoma of the colon

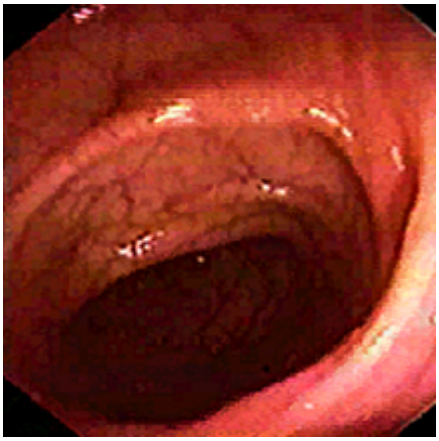


Adenocarcinoma of the colon may have a variety of appearances on endoscopy. Panel A: a typical exophytic mass; Panel B: a friable polypoid mass; Panel C: circumferential adenocarcinoma.

Courtesy of James B McGee, MD.

Graphic 74346 Version 1.0

Normal sigmoid colon

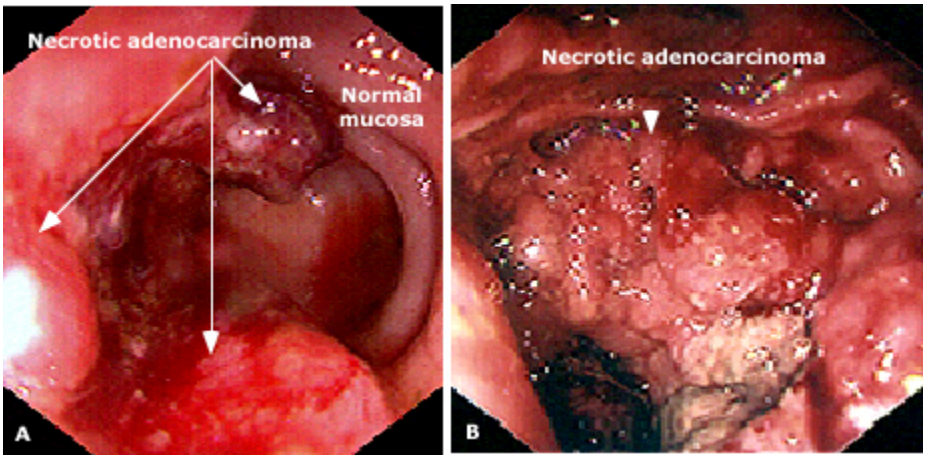


Endoscopic appearance of the normal sigmoid colonic mucosa. The fine vasculature is easily visible, and the surface is shiny and smooth. The folds are of normal thickness.

Courtesy of James B McGee, MD.

Graphic 55563 Version 1.0

Necrotic adenocarcinoma of the colon



Endoscopy showing necrotic colonic lesions that usually suggest an advanced stage of malignancy. Panel A: severe tissue destruction has led to necrosis and bleeding; Panel B: the longstanding tumor has extended deeply into the mucosa and become necrotic.

Courtesy of James B McGee, MD.

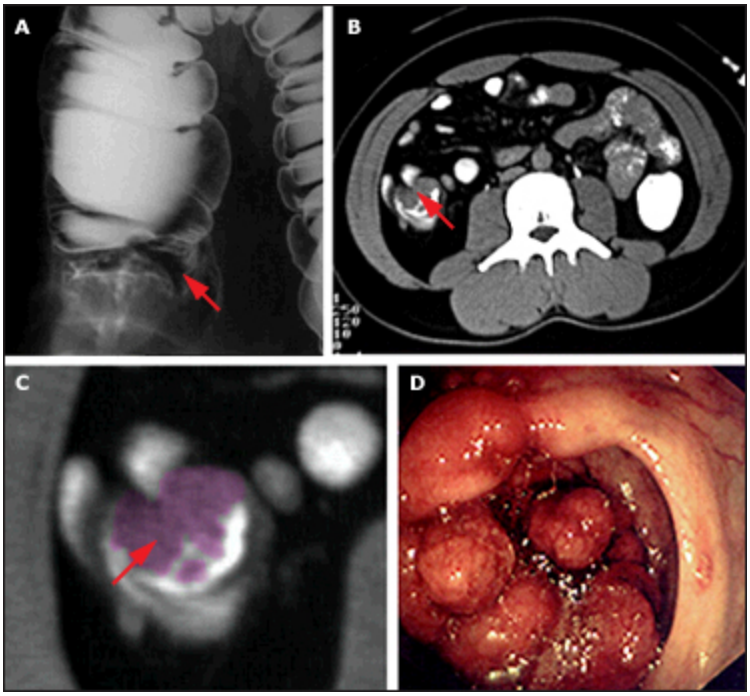
Graphic 54234 Version 1.0

Endoscopic criteria suggesting malignancy of a polyp

Firm consistency
Adherence
Ulceration
Friability

Graphic 68868 Version 1.0

Familial colon cancer



These images are from a 38-year-old man who was found to have heme positive stool. His father and two uncles died of colon cancer before the age of fifty. Panel A: The initial study was a barium enema (although a colonoscopy is more commonly used as the initial diagnostic study for heme positive stools). The barium enema reveals a filling defect in the cecum (arrow). Panels B and C: A CT scan of the abdomen shows a large exophytic mass (colored in pink in panel C) involving the cecum (arrows). Panel D: Colonoscopy reveals that the large exophytic lesion occupies most of the cecum. Adenocarcinoma was confirmed by biopsy. Despite the size of the lesion, the tumor had not spread beyond the colonic wall.

Courtesy of James B McGee, MD.

Graphic 51584 Version 2.0

Causes of a colonic mass

Malignant lesions
Adenocarcinoma
Lymphoma
Carcinoid tumor
Kaposi sarcoma
Prostate cancer
Benign lesions
Crohn colitis
Diverticulitis
Endometriosis
Solitary rectal ulcer
Lipoma
Tuberculosis
Amebiasis
Cytomegalovirus
Fungal infection
Nematode (roundworm) infection
Extrinsic lesion

Graphic 66850 Version 4.0

Colorectal cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*, intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae)
T1	Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)
T2	Tumor invades the muscularis propria
T3	Tumor invades through the muscularis propria into pericolorectal tissues
T4	Tumor invades* the visceral peritoneum or invades or adheres¶ to adjacent organ or structure
T4a	Tumor invades* through the visceral peritoneum (including gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum)
T4b	Tumor directly invades* or adheres¶ to adjacent organs or structures
* Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (ie, respectively, a tumor on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix, or vagina). ¶ Tumor that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumor is present in the adhesion, microscopically, the classification should be pT1-4a depending on the anatomical depth of wall invasion. The V and L classification should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN prognostic factor should be used for perineural invasion.	
Regional lymph nodes (N)	
N category	**N criteria**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0.2 mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative

N1a	One regional lymph node is positive
N1b	Two or three regional lymph nodes are positive
N1c	No regional lymph nodes are positive, but there are tumor deposits in the: ▪ Subserosa ▪ Mesentery ▪ Nonperitonealized pericolic, or perirectal/mesorectal tissues
N2	Four or more regional nodes are positive
N2a	Four to six regional lymph nodes are positive
N2b	Seven or more regional lymph nodes are positive

Distant metastasis (M)

M category	M criteria
M0	No distant metastasis by imaging, etc; no evidence of tumor in distant sites or organs. (This category is not assigned by pathologists.)
M1	Metastasis to one or more distant sites or organs or peritoneal metastasis is identified
M1a	Metastasis to one site or organ is identified without peritoneal metastasis
M1b	Metastasis to two or more sites or organs is identified without peritoneal metastasis
M1c	Metastasis to the peritoneal surface is identified alone or with other site or organ metastases

Prognostic stage groups

When T is…	And N is…	And M is…	Then the stage group is…
Tis	N0	M0	0
T1, T2	N0	M0	I
T3	N0	M0	IIA
T4a	N0	M0	IIB
T4b	N0	M0	IIC
T1-T2	N1/N1c	M0	IIIA
T1	N2a	M0	IIIA
T3-T4a	N1/N1c	M0	IIIB
T2-T3	N2a	M0	IIIB
T1-T2	N2b	M0	IIIB
T4a	N2a	M0	IIIC

T3-T4a	N2b	M0	IIIC
T4b	N1-N2	M0	IIIC
Any T	Any N	M1a	IVA
Any T	Any N	M1b	IVB
Any T	Any N	M1c	IVC

TNM: Tumor, Node, Metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

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Graphic 111438 Version 10.0

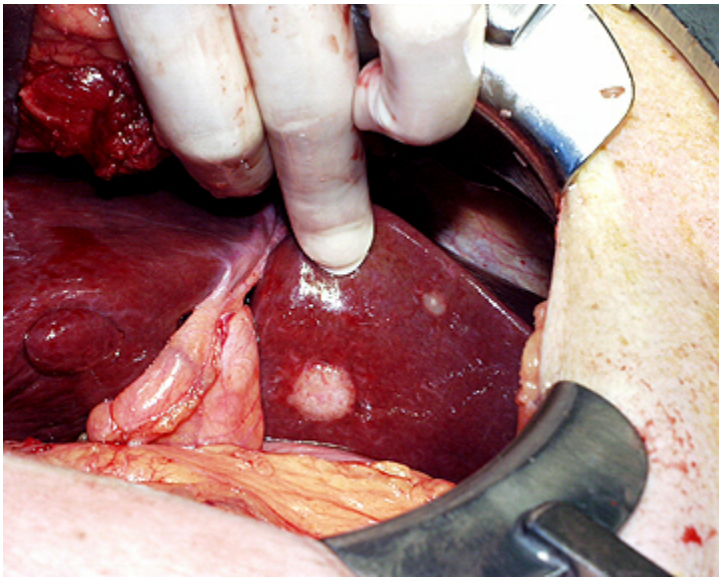
Modified Ryan scheme for tumor regression scoring in rectal cancer treated preoperatively

Description	Tumor regression score
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near-complete response)	1
Residual cancer with evident tumor regression, but more than single cells or rare small groups of cancer cells (partial response)	2
Extensive residual cancer with no evident tumor regression (poor or no response)	3

Modified from: Ryan R, Gibbons D, Hyland JM, et al. Pathological response following long-course neoadjuvant chemoradiotherapy for locally advanced rectal cancer. Histopathology 2005; 47:141. http://onlinelibrary.wiley.com/wol1/doi/10.1111/j.1365-2559.2005.02176.x/abstract. Copyright © 2005. Reproduced with permission of John Wiley & Sons Inc. This image has been provided by or is owned by Wiley. Further permission is needed before it can be downloaded to PowerPoint, printed, shared or emailed. Please contact Wiley's permissions department either via email: permissions@wiley.com or use the RightsLink service by clicking on the 'Request Permission' link accompanying this article on Wiley Online Library (http://onlinelibrary.wiley.com).

Graphic 111439 Version 1.0

Metastatic colon cancer



Multiple liver metastases seen during laparotomy in a patient with colon cancer.

Courtesy of Richard B Freeman, Jr, MD.

Graphic 81255 Version 1.0

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